CLAIMS

1. Nitrooxyderivatives or salts thereof having the following general formula (I)

$$R\text{-}\ NR_{1c}\text{-}(K)_{k0}\text{-}(B)_{b0}\text{-}(C)_{c0}\text{-}NO_2 \qquad (I)$$

wherein

c0 is 0 or 1;

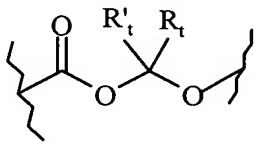
b0 is 0 or 1, with the proviso that c0 and b0 can not be simultaneously 0;

k0 is 0 or 1;

R is the radical of an analgesic drug for chronic pain;

R_{1c} being H or straight or branched alkyl with from 1 to 5 carbon atoms;

K is (CO) or the bivalent radical (1C) having the following formula:



(1-C)

wherein the carbonyl group is bound to T_1; R_t and R'_t, same or different, are H, C_1-C_{10}-alkyl, phenyl or benzyl, -$COOR_y$, in which R_y = H, C_1-C_{10}-alkyl, phenyl, benzyl;

B = -T_B-X_2-T_{BI}- wherein

T_B = (CO) or X, in which X = O, S, NH;

with the proviso that:

when b0 = 1 and k0 = 0, then T_B = (CO);

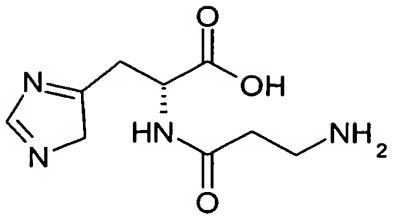
when b0 = 1 and k0 = 1, being K = (CO), then T_B = X as defined above;

T_{BI} = (CO) or (X), wherein X is as defined above;

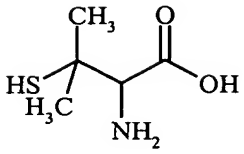
when c0 = 0, then T_{BI} = -O-;

X_2 is such a bivalent bridging group such as the corresponding precursor of B, having the formula Z-T_B-X_2-T_{BI}-Z' in which Z, Z' are independently H or OH, is selected from the following compounds:

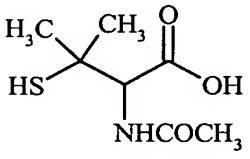
- Aminoacids: L-carnosine (CI), penicillamine (CV), N-acetylpenicillamine (CVI), cysteine (CVII), N-acetylcysteine (CVIII):



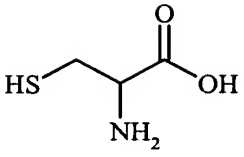
(CI)



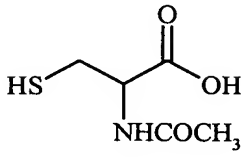
(CV)



(CVI)

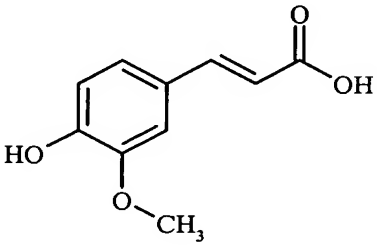


(CVII)

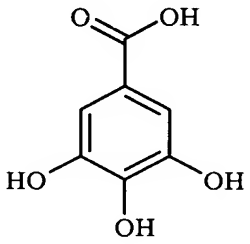


(CVIII)

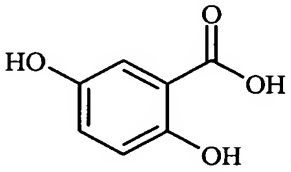
- Hydroxyacids: gallic acid (DI), ferulic acid (DII), gentisic acid (DIII), caffeic acid (DV), hydro caffeic acid (DVI), p-coumaric acid (DVII), vanillic acid (DVIII), syringic acid (DXI):



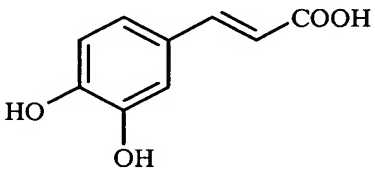
(DII)



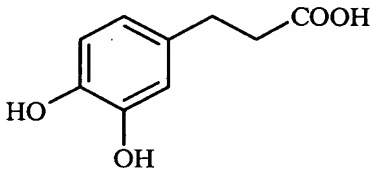
(DI)



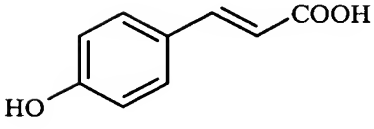
(DIII)



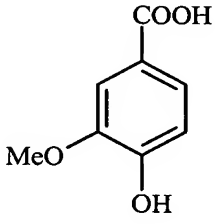
(DV)



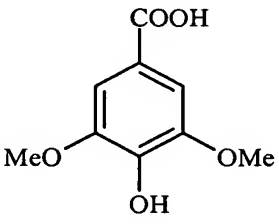
(DVI)



(DVII)

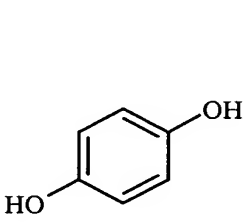


(DVIII)

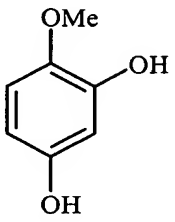


(DXI);

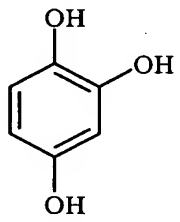
- aromatic polyalcohols: hydroquinone (EVIII), methoxyhydroquinone (EXI), hydroxyhydroquinone (EXII), conyferyl alcohol (EXXXII), 4-hydroxyphenetyl alcohol (EXXXIII), p-coumaric alcohol (EXXXIV):



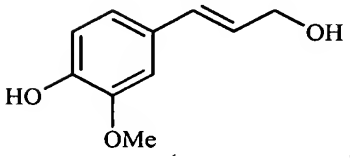
(EVIII),



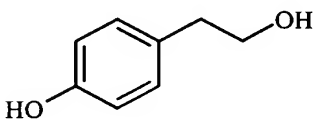
(EXI),



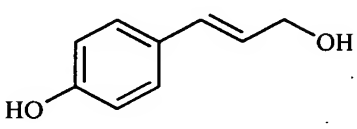
(EXII),



(EXXXII),



(EXXXIII),



(EXXXIV);

C = bivalent radical having the formula $-T_c-Y-$

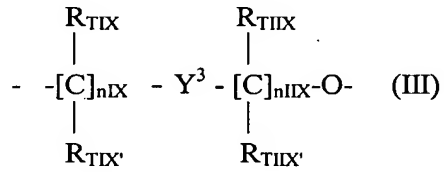
wherein

T_c = (CO) or X being as defined above;

with the proviso that when b0 =0 and k0 = 1:

- T_c = (CO) when K = (1C),
- T_c = X as defined above when K = (CO); and

Y has one of the following meanings:



(III)

wherein:

nIX is an integer of from 0 to 5;

nIIX is an integer of from 1 to 5;

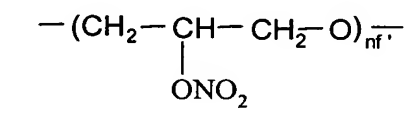
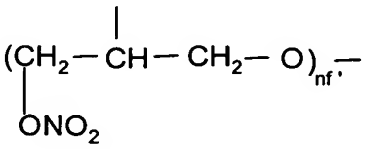
R_{TIX}, $R_{TIX'}$, R_{TIIX}, $R_{TIIX'}$, the same or different, are H or straight or branched C_1-C_4-alkyl;

Y^3 is a saturated, unsaturated or aromatic heterocyclic ring with 5 or 6 atoms, containing one to three heteroatoms, said heteroatoms being the same or different and selected from nitrogen, oxygen or sulphur;

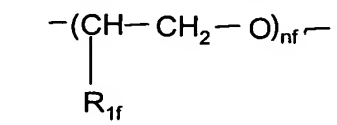
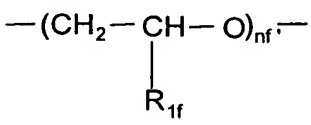
or Y may be:

an alkylenoxy group –R'O– in which R' is straight or branched C_1-C_{20} or a cycloalkylene with from 5 to 7 carbon atoms, and wherein in cycloalkylene ring one or more carbon atoms can be replaced by heteroatoms and the ring may present side chains of R' type, R' being as defined above;

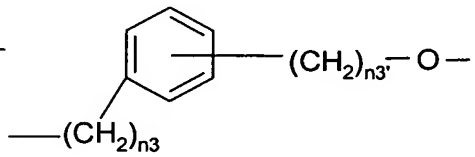
or one of the following groups:

-  ; 

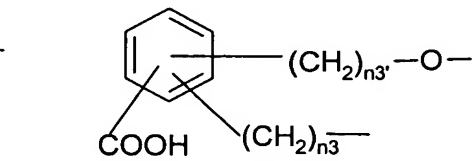
wherein nf' is an integer from 1 to 6;

-  ; 

wherein R_{1f} = H, CH_3 and nf' is an integer from 1 to 6;

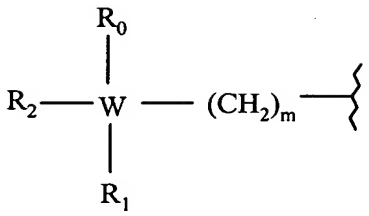
- 

wherein n3 is an integer from 0 to 5 and n3' is an integer from 1 to 3; or

- 

in which n3 and n3' have the meaning mentioned above;

R is the radical of an analgesic drug having formula (II):



(II)

wherein:

W is a carbon or nitrogen atom;

m is an integer of from 0 to 2;

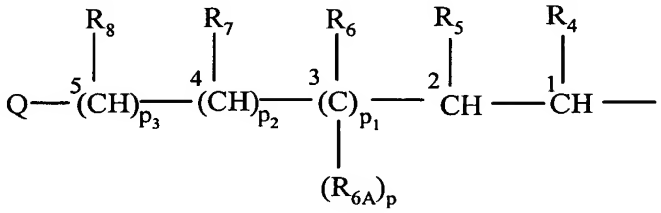
R_0 = H, $-(CH_2)_n-COOR_y$, R_y being as defined above;

n is an integer of from 0 to 2;

R_1 = H; when W = N, R_1 is the electronic doublet on nitrogen atom (free valence);

R_2 is selected from the following groups:

- phenyl, optionally substituted with a halogen atom or with a group selected from $-OCH_3$, $-CF_3$, nitro;
- mono or dihydroxy-substituted benzyl, preferably 3,4-dihydroxybenzyl;
- amidino group: $H_2N(C=NH)-$;
- a radical of formula (IIA), wherein optionally an ethylenic unsaturation may be present between the carbon atoms in position 1 and 2, or 3 and 4 or 4 and 5:



(IIA)

wherein:

p, p_1, p_2 are integers, same or different, and are 0 or 1;

p_3 in an integer of from 0 to 10;

R_4 is hydrogen, straight or branched C_1-C_6-alkyl, free valence;

R_5 may have the following meanings:

- hydrogen,
- straight or branched C_1-C_6-alkyl,
- C_3-C_6-cycloalkyl,
- OR_A, R_A having the following meanings:

- straight or branched C_1-C_6-alkyl, optionally substituted with one or more halogen atoms, preferably F,
- phenyl optionally substituted with a halogen atom or with one of the following groups: $-OCH_3$, $-CF_3$, nitro;

R_6, R_{6A}, R_7, R_8, the same or different, are H, methyl or free valence, with the proviso that when an ethylenic unsaturation is present between C_1 and C_2 in radical of formula (IIA), R_4 and R_5 are free valences able to form the double bond between C_1 and C_2; if the unsaturation is between C_3 and C_4, R_6 and R_7 are free valence able to form the double bond between C_3 and C_4; is the unsaturation is between C_4 and C_5, R_7 and R_8 are free valence able to form the double bond between C_4 and C_5;

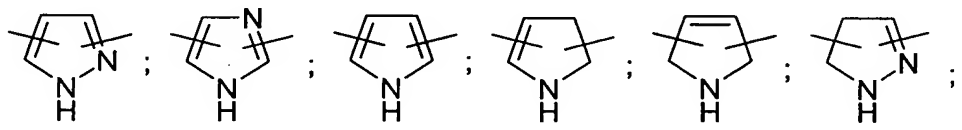
Q is H, OH, OR_B, R_B being benzyl, straight or branched C_1-C_6-alkyl, optionally substituted with one or more halogen atoms, preferably F, phenyl optionally substituted with a halogen atom or with one of the following groups: $-OCH_3$, $-CF_3$, nitro; or

Q may have one of the following meanings:

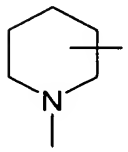
- straight or branched C_1-C_6-alkyl,
- C_3-C_6-cycloalkyl,
- guanidino ($H_2NC(=NH)NH$-),
- thioguanidino ($H_2NC(=S)NH$-).

in formula (II) R_2 with R_1 and with W = C form together a C_4-C_{10} saturated or unsaturated ring.

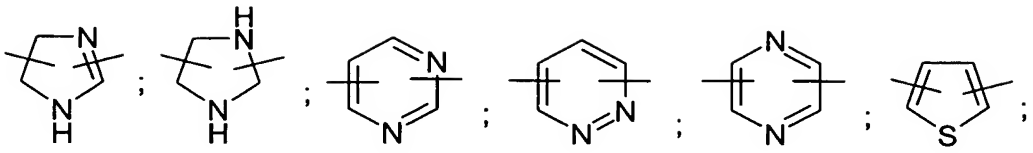
2. Compounds according to claim 1, characterized in that Y^3 in formula (III) is selected from:



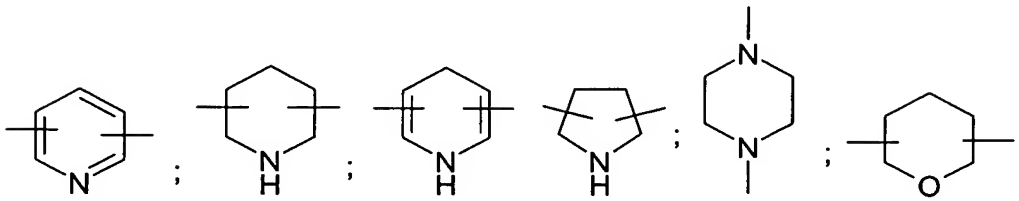
(Y1) (Y2) (Y3) (Y4) (Y5) (Y6)



(Y19)



(Y7) (Y8) (Y9) (Y10) (Y11) (Y18)



(Y12) (Y13) (Y14) (Y15) (Y16) (Y17)

3. Compounds according to claim 1, characterized in that in formula (I):

c0 is 1;

b0 is 0 or 1;

k0 is 0 or 1;

R_{1c} = H;

K is (CO) or the bivalent radical (1C) as defined in claim 1;

B = $-T_B-X_2-T_{BI}-$ wherein

T_B = (CO) or X, in which X = O, S, NH;

with the proviso that:

when b0 = 1 and k0 = 0, then T_B = (CO);

when b0 = 1 and k0 = 1, being K = (CO), then T_B = X as defined above;

T_{BI} = (CO) or (X), wherein X is as defined above;

when c0 = 0, then T_{BI} = -O-;

the precursor of B is N-acetylcysteine or ferulic acid;

C = bivalent radical having the formula $-T_c-Y-$

wherein

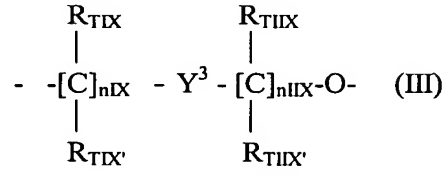
T_c = (CO) or X being as defined above;

with the proviso that when b0 =0 and k0 = 1:

- T_c = (CO) when K = (1C),

- T_c = X as defined above when K = (CO); and

Y has one of the following meanings:



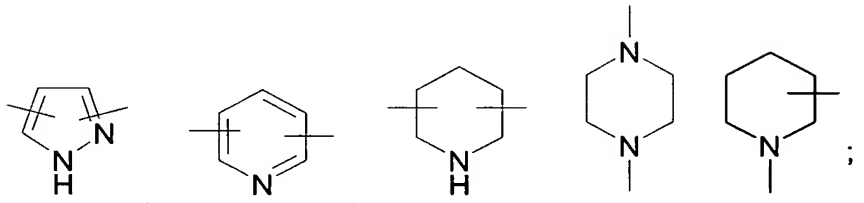
(III)

wherein:

nIX and nIIX are 1;

R_{TIX}, $R_{TIX'}$, R_{TIIX}, $R_{TIIX'}$ are H;

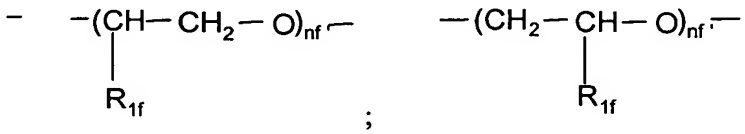
Y^3 is selected from the following bivalent radicals:



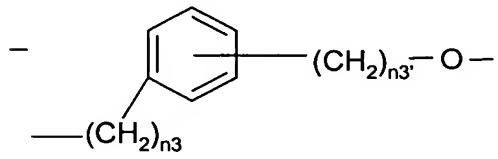
(Y1) (Y12) (Y13) (Y16) (Y19)

or Y may be:

an alkylenoxy group –R'O– in which R' is straight or branched C_2-C_6 alkyl; or

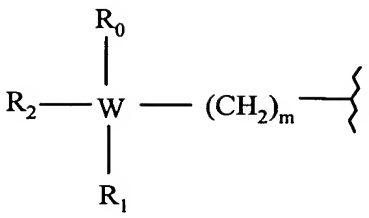


wherein R_{1f} = H, CH_3 and nf' is an integer from 1 to 4;



wherein n3 is an integer from 0 to 3 and n3' is an integer from 1 to 3;

R is the radical of an analgesic drug having formula (II):



(II)

wherein:

W is a carbon atom;

m is 0 or 1;

R_0 = H or -$(CH_2)_n$-COOH, wherein n is an integer of from 0 to 2;

R_1 = H;

R_2 is selected from the following groups:

- 3,4-dihydroxybenzyl; or
- a radical of formula (IIA) as defined in claim 1, wherein:

p and p_1 are are 0 or 1;

p_2 and p_3 are 0;

R_4 and R_5 are hydrogen, straight or branched C_1-C_6-alkyl or free valence;

R_6 and R_{6A} are H;

with the proviso that when an ethylenic unsaturation is present between C_1 and C_2 in radical of formula (IIA), R_4 and R_5 are free valences able to form the double bond between C_1 and C_2;

Q is H, CH_3 or

- guanidino ($H_2NC(=NH)NH$-), or
- thioguanidino ($H_2NC(=S)NH$-);

in formula (II) R_2 with R_1 and with W form together a C_6 saturated ring.

4. Compounds according to claims 1-3, wherein when in formula (II) W = C, m = 1 and R_0 = -$(CH_2)_n$-$COOR_y$, wherein n = 1 and R_y = H; R_2 and R_1 with W as defined above form the cyclohexane ring; the drug precursor of R having the formula R-NH_2 is known as gabapentin;

when in formula (II) W = C, m = 0 and R_0 if defined as for gabapentin with n = 0; R_1 = H; R_2 is the radical of formula (IIA) in which p = p_1 = 1, p_2 = p_3 = 0, R_4 = R_5

$= R_6 = R_{6A} = H$, Q = H; the drug precursor of R having the formula $R\text{-}NH_2$ is known as norvaline;

when in formula (II) W = C, m = 0 and R_0 if defined as for gabapentin with n = 0; R_1 = H; R_2 is the radical of formula (IIA) in which $p = p_1 = 1$, $p_2 = p_3 = 0$, $R_4 = R_5 = R_6 = R_{6A}$ = H, Q is the guanidino group; the drug precursor of R having the formula $R\text{-}NH_2$ is known as arginine;

when in formula (II) W = C, m = 0 and R_0 if defined as for gabapentin with n = 0; R_1 = H; R_2 is the radical of formula (IIA) in which $p = p_1 = 1$, $p_2 = p_3 = 0$, $R_4 = R_5 = R_6 = R_{6A}$ = H, Q is the thioguanidino group; the drug precursor of R having the formula $R\text{-}NH_2$ is known as thiocitrulline;

when in formula (II) W = C, m = 1 and R_0 if defined as for gabapentin with n = 1; R_1 = H; R_2 is the radical of formula (IIA) in which $p = p_1 = p_2 = p_3 = 0$, R_4 = H, $R_5 = Q = CH_3$; the drug precursor of R having the formula $R\text{-}NH_2$ is known as pregabalin;

when in formula (II) W = C and has (S) configuration, m = 1 and R_0 if defined as for gabapentin with n = 1; R_1 = H; R_2 is the radical of formula (IIA) in which $p = p_1 = p_2 = p_3 = 0$, R_4 = H, $R_5 = Q = CH_3$; the drug precursor of R having the formula $R\text{-}NH_2$ is known as (S)3-isobutilGABA;

when in formula (II) W = C and has (S), m = 0; $R_0 = R_1$ = H; R_2 is the radical of formula (IIA) in which $p = p_1 = 1$, $p_2 = p_3 = 0$, $R_4 = R_5 = R_6 = R_{6A}$ = H, Q is the guanidino group; the drug precursor of R having the formula $R\text{-}NH_2$ is known as agmatine;

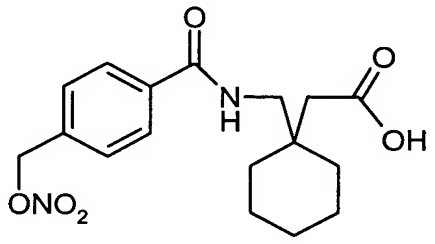
when in formula (II) W = C, m = 0; R_0 if defined as for gabapentin with n = 2; R_1 = H; R_2 is the radical of formula (IIA) in which $p = p_1 = p_2 = p_3 = 0$, R_4 and R_5 are free valences and between C_1 and C_2 there is an ethylenic unsaturation, Q = H; the drug precursor of R having the formula $R\text{-}NH_2$ is known as vigabatrin;

when in formula (II) W = C, m = 0; R_0 if defined as for gabapentin with n = 0; R_1 = H; R_2 is the 3,4-dihydroxybenzyl radical; the drug precursor of R having the formula $R\text{-}NH_2$ is known as 2-amino-3-(3,4-dihydroxyphenylpropanoic acid (dopa).

5. Compounds according to claims 1-3, wherein the drug precursors of R in formula (I) are selected from lamotrigine, topiramate, zonisamide, carbamazepine, felbamate, amineptine, amoxapine, demexiptiline, desipramine, nortriptyline, tianeptine.

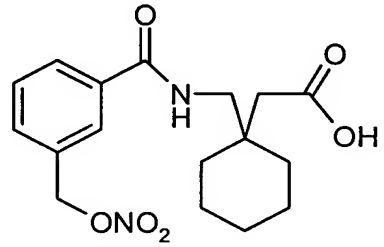
6. Compounds according to claims 1, 3 and 4 selected from:

1-[4-(nitrooxymethyl)benzoylaminomethyl]-cyclohexaneacetic acid (XVA),



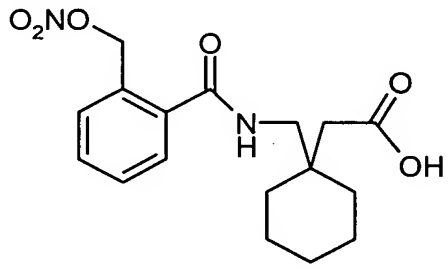
(XVA)

1-[3-(nitrooxymethyl)benzoylaminomethyl]-cyclohexaneacetic acid (XVIA),



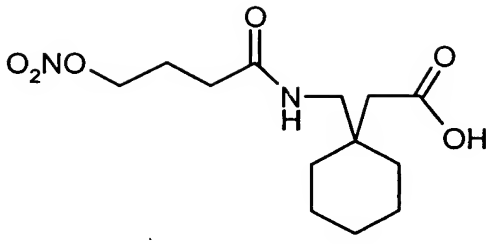
(XVIA)

1-[2-(nitrooxymethyl)benzoylaminomethyl]-cyclohexaneacetic acid (XVIIA),



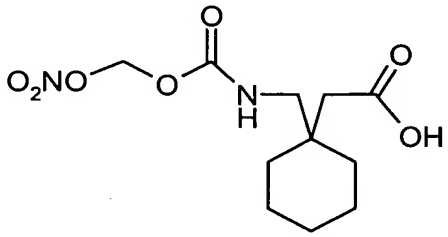
(XVIIA)

1-(4-nitrooxybutanoylaminomethyl)-cyclohexaneacetic acid (XVIIIA),



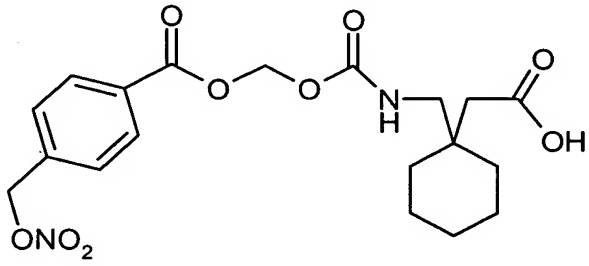
(XVIIIA)

1-(nitrooxymethoxycarbonylaminomethyl)-cyclohexaneacetic acid (XIXA),



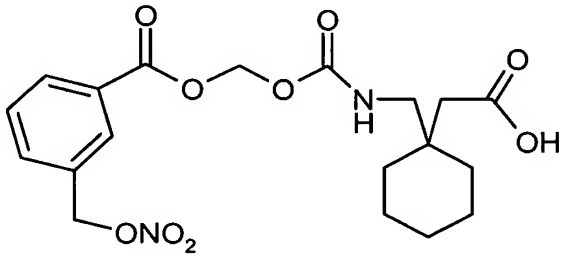
(XIXA)

1-{[4-(nitrooxymethyl)benzoyloxy]methoxycarbonylaminomethyl}-cyclohexaneacetic acid (XXA),



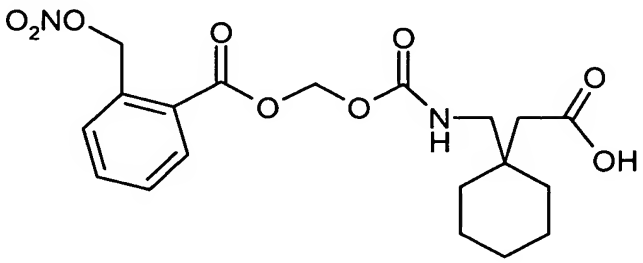
(XXA)

1-{[3-(nitrooxymethyl)benzoyloxy]methoxycarbonylaminomethyl}-cyclohexaneacetic acid (XXIA),



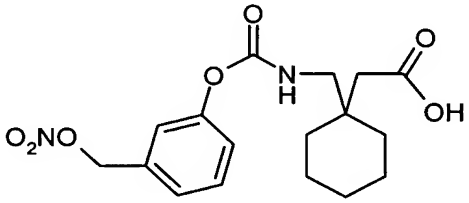
(XXIA)

1-{[2-(nitrooxymethyl)benzoyloxy]methoxycarbonylaminomethyl}-cyclohexaneacetic acid (XXIIA),



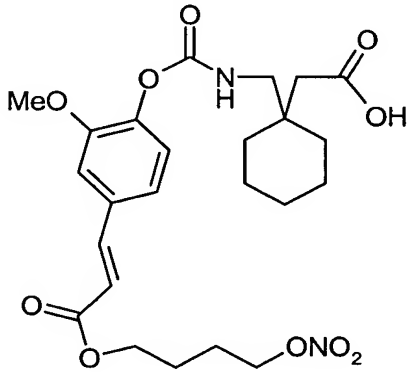
(XXIIA)

1-[3-(nitrooxymethyl)phenoxycarbonylaminomethyl]-cyclohexaneacetic acid (XXIIIA),



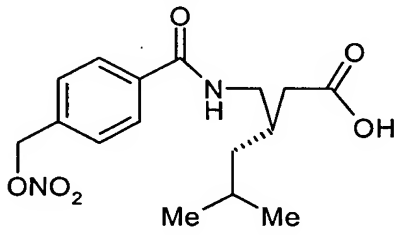
(XXIIIA)

{2-methoxy-4-[(1E)-3-[4-(nitrooxybutoxy)-3-oxa-1-propenylphenoxy]-carbonylamino-methyl}-cyclohexaneacetic acid (XXIVA),



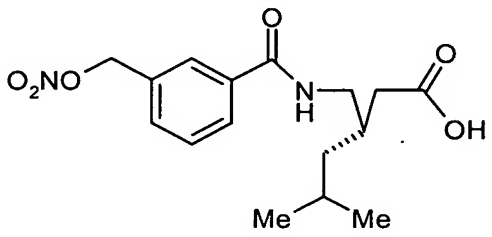
(XXIVA)

3-(S)-[4-(nitrooxymethyl)benzoylaminomethyl]-5-methyl-hexanoic acid (XXVA),



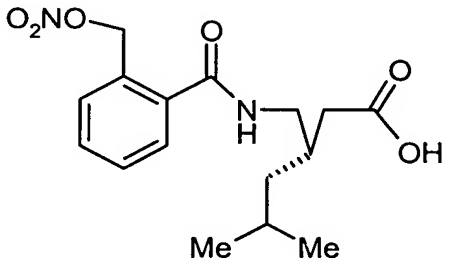
(XXVA)

3-(S)-[3-(nitrooxymethyl)benzoylaminomethyl]-5-methyl-hexanoic acid (XXVIA),



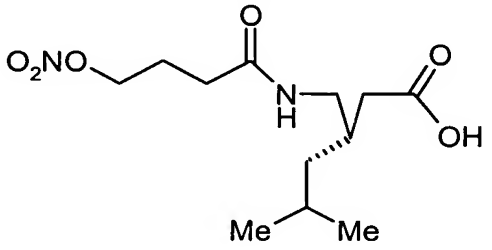
(XXVIA)

3(S)-[2-(nitrooxymethyl)benzoylaminomethyl]-5-methyl-hexanoic acid (XXVIIA),



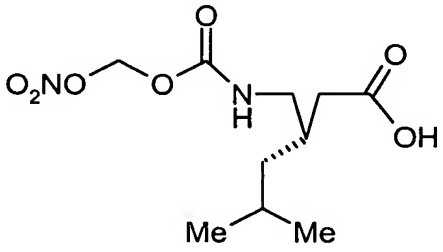
(XXVIIA)

3(S)-[4-(nitrooxybutanoyl)aminomethyl]-5-methyl-hexanoic acid (XXVIIIA),



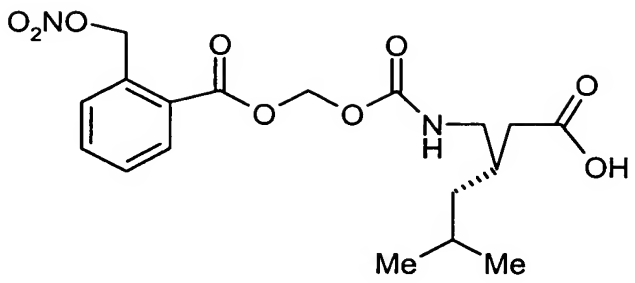
(XXVIIIA)

3(S)-[4-(nitrooxymethoxycarbonyl)aminomethyl]-5-methyl-hexanoic acid (XXIXA),



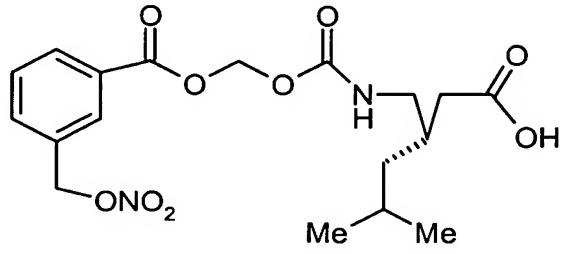
(XXIXA)

3(S)-{[2-(nitrooxymethyl)benzoyloxy]methoxycarbonylaminomethyl}-5-methyl-hexanoic acid (XXXA),



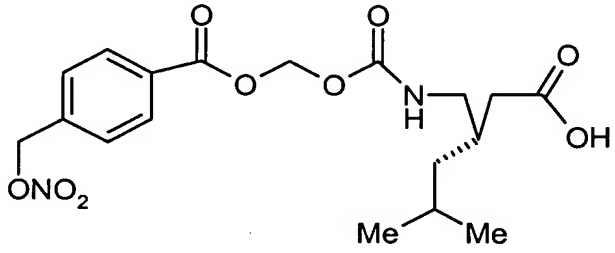
(XXXA)

3(S)-{[3-(nitrooxymethyl)benzoyloxy]methoxycarbonylaminomethyl}-5-methyl-hexanoic acid (XXXIA),



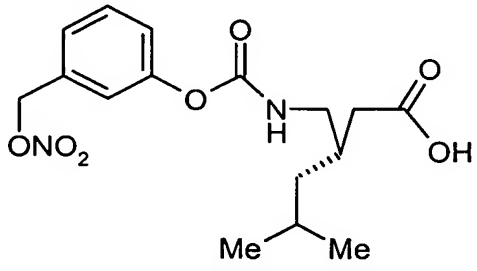
(XXXIA)

3(S)-[4-(nitrooxymethyl)benzoyloxy]methoxycarbonylaminomethyl}-5-methyl-hexanoic acid (XXXIIA),



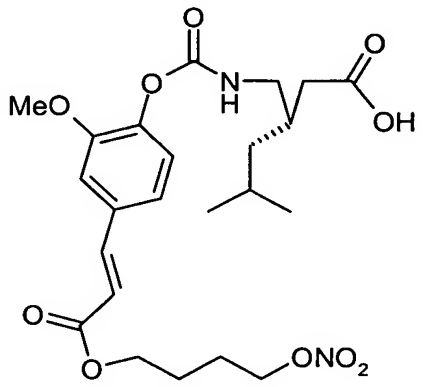
(XXXIIA)

3(S)-[(3-nitrooxymethyl)phenoxycarbonylaminomethyl]-5-methyl-hexanoic acid (XXXIIIA),



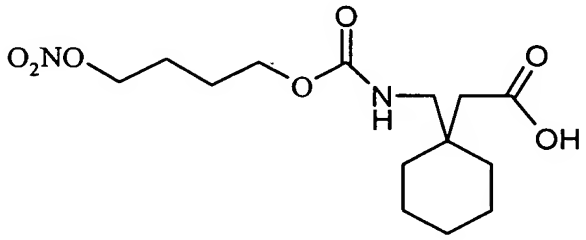
(XXXIIIA)

3(S)-{2-methoxy-4-[(1E)-3-[4-(nitrooxybutoxy]-3-oxa-1-propenylphenoxy]carbonyl-aminomethyl}-5-methyl-hexanoic acid (XXXIVA),



(XXXIVA)

1-[4-(nitrooxybutyloxycarbonyl)aminomethyl]-cyclohexaneacetic acid (XXXVA),



(XXXVA)

7. Compounds according to claims 1-6, in combination with NO-donor compounds.

8. Compounds according to claim 7, wherein the NO-donors contain in the molecule radicals of the following drugs: aspirin, salicylic acid, ibuprofen, paracetamol, naproxen, diclofenac and flurbiprofen.

9. Pharmaceutical compositions comprising compounds according to claims 1-8 as active ingredients.

10. Compounds according to claims 1-8 to be employed as a drug.

11. Use of the compounds according to claims 1-8 for preparing drugs for chronic pain.

12. Use of the compounds according to claim 11, wherein the chronic pain is neurophatic pain.